JPRS: 4316

6 January 1961

THE FIRST INTERNATIONAL CONFERENCE ON CARDIO-VASCULAR SUBSTANCES

-USSR-

By A. S. Sadykov

Distributed by:

OFFICE OF TECHNICAL SERVICES
U. S. DEPARTMENT OF COMMERCE
WASHINGTON 25, D. C.

U. S. JOINT PUBLICATIONS RESEARCH SERVICE
1636 CONNECTICUT AVENUE, N. W.
WASHINGTON 25, D. C.

F O R E W O R D

This publication was prepared under contract by the UNITED STATES JOINT PUBLICATIONS RESEARCH SERVICE, a federal government organization established to service the translation and research needs of the various government departments.

JPRS: 4316

CSO: 1326-S

THE FIRST INTERNATIONAL CONFERENCE ON CARDIO-VASCULAR SUBSTANCES

-USSR-

/The following is a translation of the article "I Mezhdunarodnaya konferentsiya po serdechno-sosudistym veshchestvam," by A. S. Sadykov in Uzbekskiy Khimicheskiy Zhurnal (Uzbek Chemical Journal), No 4, Tashkent, 1960, pages 67-70./

On the invitation of the Department of Organic Chemistry of the Chemical Institute of the Slovak Academy of Sciences, the First International Conference on Cardio-Vascular Substances took place from 25-28 November 1959, in Smolenice. Taking part in the Conference were scientists from the German Democratic Republic, Hungary, Poland, the Soviet Union, Austria, the Federal Republic of Germany and others.

The problem of cardio-vascular substances has at present exceptionally important significance and takes in a wide number of chemical, biochemical and physiological questions.

Glucosides, alkaloids and other organic substances have for a long time been employed in medicine as medicinal agents.

Participants in the Conference heard 57 reports on the chemistry, pharmacology and the clinical use of glucosides and alkaloids (natural and synthetic fragments of indole alkaloids) which as a guide may be systematized in the following manner: a) the isolation and study of organic cardio glucosides; b) the isolation and study of organic alkaloids and their pharmacology; c) synthetic research of analogues and models of indole alkaloids; d) organic compounds possessing hypotensive activity; and, e) reports on general questions of chemical therapy and the clinical use of cardio-vascular substances.

Of particular interest were the reports of G. Bardos and others (Bratislava) on "The Activity of the Parasympatholytic and Parasympathomimetic Substances on

the Process of the Physiological Enlarging of the Heart;" G. Raskova (Prague) on "Clinical Research on New Medicines," and O. Repka and others (Prague) on "Clinical Testing of Substances which Reduce Blood Pressure."

The report of S. Bauer (Department of Organic Chemistry of the Slovek Academy of Sciences) was full of much factual material on the study of the glucosides of the plant families Brassicaceae, Scrophyllariaceae, Papillionaceae, Ronunculaceae and others.

D. Sikl isolated from the leaves of the May lily of the valley (Convallaria majalis L.) by the method of counterflow shaking a glucoside convallarotoxin. He discovered as well a new glucoside with definite physicochemical properties. In addition he studied the dynamics of the accumulation and changes of the convallatoxin in the leaves of the lily of the valley depending upon the period of picking, the growing place and other soil and climatic conditions.

S. Orsang shared his results of the isolation of the glucoside helveticoside from the Erysimum canescens yielding 0.1 - 0.2% by the method of aqueous extraction from organic matter with a mixture of chloroform -- methanol, and by shaking it with a mixture of toluene -- n-butyl alcohol -- water after the thickening of the extract. After the extraction of the solvent under vacuum and crystallization, the crystallized helveticoside was received.

I. Korbelar told of the therapeutic experience with helveticoside glucoside with cardiotonic effect.

A. Babul'ova and F. Seletskiy, speaking on the cardiotoxic and cardiotonic effects of helveticoside, brought out comperative data on heveticoside with strophanthin and convallatoxin. The cardiotonic effect of the glucoside was determined on the isolated heart and on the cardio-pulmonary system of frogs and rabbits.

In the address of O. Gorakov and others (Bratislava) data were given on the glucoside helleborin extracted from domestic Helleborus purpurascens (yield 0.2%). The substance has been compared with the helleborin received from H. niger, and their identity has been proven. The cardiotonic effect of helleborin has been established in various solvents. In addition to helleborin an undescribed glucoside with a mol. wt. 242° was extracted by the method of a paper chromatograph.

G. Kecova (Prague) told about the most recent preparations extracted from Digitalis lanata (acetyldigitoxin, lanatoside, desacetyllanatoside S).

On the instructions of the scientists of the Khar'kov Scientific Research Chemical-Pharmaceutical Institute,

M. A. Angarskaya spoke on the results of the comparative pharmacological characteristics of new cardio glucosides -- sireniotoxin, alloiside, homphtine and hophruside, all of which have shown significant biological effects.

A very interesting report was given by the colleagues of the Department of Organic Chemistry of the Chemical Institute of the Slovak Academy of Sciences on the chemistry and pharmacology of the alkaloids from Veratrum album L.

In the report of I. Tomko, C. Bauerov, and I. Bendik data were brought forth on the isolation and extraction of the alkaloids of V. album growing in Slovakia. It was shown the the plant does not contain protoveratrine. Several new alkaloids were isolated with a complex ether character and with significant hypotensive effect. By the method of the chromatograph three more bases were discovered with hypotensive characteristics.

The report of V. Ditteovaya and F. Seletskiy was devoted to the questions of the study of the hypotensive activity of separate fractions and to the establishing of their effect.

O. Strauf and others (Scientific Research Institute of Medicinal Plants, Prague) devoted their reports to a survey of the isolation and fractional separation of the sum of alkaloids from Vinca minor (growing in Czechoslovakia) with the isolation of vincamine, isovincamine, vincaminoreine, and vincamidine. They reported on the detailed physico-chemical properties of the isolated bases. I. Krejci and others showed that vincamine possesses good hypotensive effect when administered in doses of radiation of 100 gamma/kg. Higher doses significantly influence the activity of the heart and breathing. Further study on vincamine has given new data on the regulation of blood pressure.

J. Mokra and I. Kompis (Department of Organic Chemistry of the Chemical Institute of the Slovak Academy of Sciences) gave a survey of the alkaloids extracted from Vinca minor, and brought out data on the separation of the sum of bases and the extraction of vincamine, isovincamine, a new means for extracting vincaminorine and a detailed characterization of an undescribed alkaloid vincarine and four more crystallized bases.

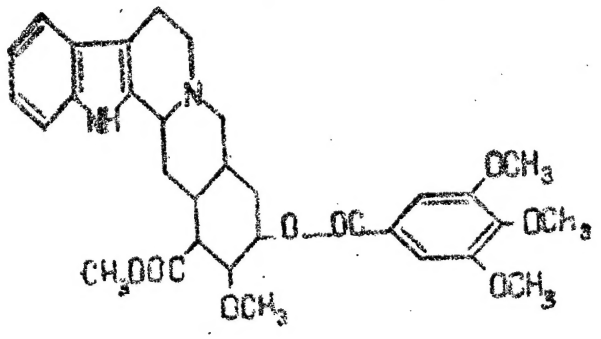
Worthy of note were the speeches of the chemists and pharmacologists (Scientific Research Institute of Pharmacy and Biochemistry, Prague) which were devoted to the synthetic research of alkaloids of Rauwolfia and to producing norharman, and in particular to the chemical and pharocological research of the indole which they

produced. In the opinion of L. N. Yakhontov (Uspekhi Khemii (Successes in Chemistry), No 26, 1957, page 239), the alkaloids of various types of Rauwolfia are related to the produced indole and are subdivided into three large groups: 1) the strong bases (quaternary anhydrous); 2) bases of medium strength (indolines); and, 3) weak bases (indoles). The indole alkaloids in their turn are divided into two groups: 1) alkaloids of the type tetrahydroalstonine; and,2) the type yohimbine. To the latter are related many of the alkaloids of Rauwolfia, for example reserpine and its stereoisomer racemidine, methylreserpate, and its isomer seredine, and also recanescine, deserpidine (identified with conessine), rescinnamine, yohimbine (its isomer) and ajmaline. The most important alkaloid of this group is reserpine which was first isolated in 1952. Its structure was discovered in 1954.

In 1956, Woodward and associates completely synthesized reserpine (Journal of American Chemical Society, No 78, 1956, page 2023).

Recanescine and conessine (deserpidine) are 11-desmethoxireserpine alkaloids. The structure of deserpidine, just as with reserpine, was discovered by research on the products of alkaline saponification (methylated alcohol, 3,4,5-trimethoxibenzoic and conessine acids), and and dehydration with selenium (iobirine). The data of the infra-red spectrum and chemical comparison show that deserpidine is a 11-desmethoxireserpine, and has the latter's configuration.

Ya. Voyknet brought attention to the fact that after the synthesis of reserpine, there began the synthetic research on the alkaloids of Rauwolfia. The scientists in the laboratory of the speaker had completely synthesized racemic deserpidine, i.e., desmethoxireserpine:

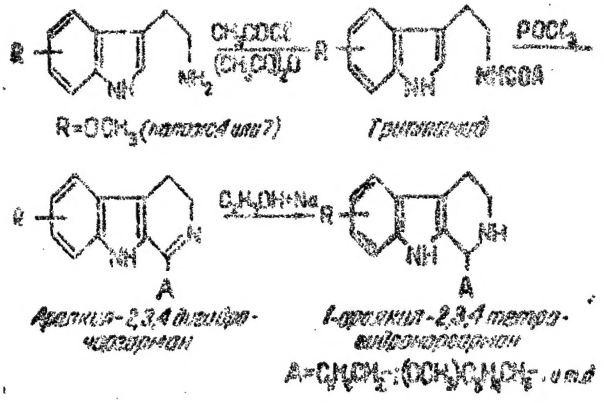


The extraction of intermediate products and of deserpine was significantly increased.

The racemism of deserpidine was split on the optical antipodes with the aid of d-camphosulphonic acid, and l-deserpidine was received, identical with the natural alkaloid, and a synthesis of isodeserpidine was realized which was distinguished from deserpidine by the steric placement of the third carbon atom. Pharmacological study of deserpidine and other synthetic models of reserpine-like alkaloids has shown that the weak influence of the methoxi-group in C_{11} on the pharmacological effect attests to the closeness of deserpidine with reserpine.

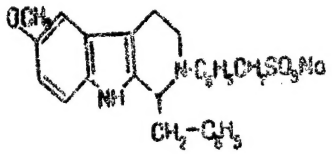
M. Protiva has shown that tryptamine and a few of its simple by-products (serotonine, psilocybine, bufotenine) are natural and pharmacologically interesting compounds. A fragment of tryptamine is met with in many alkaloids having great importance (ergotamine, yohimbine, reserpine, physostigmine, corynanthine, etc.). In the reaction of condensation of N-methyl-tryptamine with the oxide of alkylene or hydride reduction of N-methyl-tryptamine and monoethers of aliphatic dibasic acids, were received N-methyl-tryptaminoalkynoles, and 3,4,5-trimethoxibenzoic ethers which turned out to have the shape of reserpine.

In a series of syntheses, tryptamine was used as a source product. For example, as the result of the reaction of typtamine with glyoxalic acid were received the products 1,2,3,4-tetrahydroncrharman. By the cyclization of tryptamides of araliphatic acids (Collection of the Czechoslovakian Chemical Community, No 24, 1959, page 74), according to Bisler-Napiral'skiy, with the following reaction was synthesized a series of 1-substituting 2,3,4-tetrahydronorharmon according to the scheme:

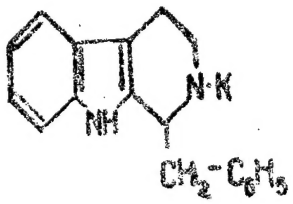


Legend: 1. R=OCH_3 (place 4 or 7); 2. tryptamide; 3. aralkyl-2,3,4 dihydronorharman; 4. 1-aralkyl-2,3,4 tetrahydronorharman.

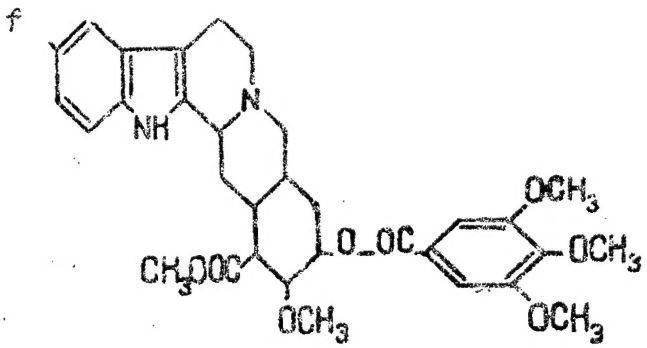
One of the preparations -- methylsulphonate 1-benzyl-2,3,4-tetrahydronorharman (phencharman) -- was used experimentally in the clinic as a sedative (of the reserpine type):



V. Trcka and M. Vanecec spoke about the testing of the preparations -- analogues of reserpine which had been synthesized by M. Protiva and his colleagues. One of the products 1,2,3,4-tetrahydronorharman, and especially 1-benzyl-2,3,4-tetrahydronorharman possesses hypotonic properties of the reserpine type:



From the compounds showing closer activity to reserpine is related the 10-florinereserpidine compound (L. Novak, M. Protiva, Naturwissenschaften, No 46, 1959, page 579), d,l-10 florinereserpidine:



Legend: 1. d,l-10 florinereserpidine.

L. Vrbovski (Chemical Institute of the Slovak Academy of Sciences) spoke on the anti-arrhythmic effect of several aliphatic ethers of abietinic and dehydro-abietinic acids. Arrhythmia was produced by the injection of barium chloride and aconitine.

M. Gava and others, and also I. Trajanec and others (Scientific Research Institute of Medicinal Plants) speaking on the hypotensive activity of the methylamide of camphoric acid in doses of 0.1 to 10 mg, brought out data on the synthesis of nitrous analogues of camphoric acid, particularly N-substituted camphidine, and also data on the conformation of the produced compounds.

In his general report, Professor A. M. Rusanov (Central Institute of Medical Radiology, Leningrad) told of the study of various camphidines which had been synthesized by the chemists of the Institute.

K. Yakimovska (Warsaw) gave a report on the bor-organic compounds of the aromatic kind. In the example of phenylboric acid and similar substances possessing depressive effects on the central nervous system, a small toxicity of the synthesized compounds was discovered.

Characterstic of the Conference was the complexity of presentation and discussion of the chemical as well as the pharmacological reports. One could thus receive a full impression of the suitability of one and another preparation for curing heart ailments.

One particularly feels like emphasizing the atmosphere of creative cooperation and mutual understanding which permeated the work of the Conference. Tribute must be paid to the organizers of the Conference -- the Slovak Academy of Sciences whose members created all conditions for mature deliberation of the participants. One must also say that the Soviet scientists profited from the extreme attention and care shown them by the Slovak colleagues.

10,272

-END-